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09/745,167 19 December 2000 (19.12.2000) US
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**WO 02/050244 A3**

(54) Title: ANTISENSE MODULATION OF HISTONE DEACETYLASE 1 EXPRESSION

(57) Abstract: Antisense compounds, compositions and methods are provided for modulating the expression of Histone deacetylase 1. The compositions comprise antisense compounds, particularly antisense oligonucleotides, targeted to nucleic acids encoding Histone deacetylase 1. Methods of using these compounds for modulation of Histone deacetylase 1 expression and for treatment of diseases associated with expression of Histone deacetylase 1 are provided.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/46518

<p><b>A. CLASSIFICATION OF SUBJECT MATTER</b>                  IPC(7) : C07H 21/00; C12Q/1/68                  US CL : 514/44; 435/6, 325, 375; 536/23.1, 24.5                  According to International Patent Classification (IPC) or to both national classification and IPC</p>											
<p><b>B. FIELDS SEARCHED</b>                  Minimum documentation searched (classification system followed by classification symbols)                  U.S. : 514/44; 435/6, 325, 375; 536/23.1, 24.5                  Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched                  Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)                  West, Biosis, CA, Medline, SciSearch</p>											
<p><b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b></p> <table border="1"> <thead> <tr> <th>Category *</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>Y --- A</td> <td>US 5,763,182 A (NAKAMURA et al) 9 June 1998 (09.06.1998) Abstract, SEQ ID No. 2, Columns 4-6.</td> <td>1, 2 ----- 3-20</td> </tr> <tr> <td>Y --- A</td> <td>TAYLOR et al. Antisense Oligonucleotides: A Systematic High-Throughput Approach to Target Validation and Gene Function Determination. Drug Discovery Today. December 1999, Vol. 4, No. 12, pages 562-567.</td> <td>1-2 ----- 3-20</td> </tr> </tbody> </table>		Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	Y --- A	US 5,763,182 A (NAKAMURA et al) 9 June 1998 (09.06.1998) Abstract, SEQ ID No. 2, Columns 4-6.	1, 2 ----- 3-20	Y --- A	TAYLOR et al. Antisense Oligonucleotides: A Systematic High-Throughput Approach to Target Validation and Gene Function Determination. Drug Discovery Today. December 1999, Vol. 4, No. 12, pages 562-567.	1-2 ----- 3-20	
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<p><input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.</p>											
<p>* Special categories of cited documents:</p> <table border="0"> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</td> </tr> <tr> <td>"B" earlier application or patent published on or after the international filing date</td> <td>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</td> </tr> <tr> <td>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</td> <td>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td>"Z" document member of the same patent family</td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>		"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	"B" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	"O" document referring to an oral disclosure, use, exhibition or other means	"Z" document member of the same patent family	"P" document published prior to the international filing date but later than the priority date claimed	
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<p>Date of the actual completion of the international search                  04 November 2002 (04.11.2002)</p>	<p>Date of mailing of the international search report                  14 AUG 2003</p>										
<p>Name and mailing address of the ISA/US                  Commissioner of Patents and Trademarks                  Box PCT                  Washington, D.C. 20231                  Facsimile No. (703)305-3230</p>	<p>Authorized officer                  Felicia D. Roberts for                  U. Douglas Schultz                  Telephone No. 703-308-1235</p>										

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/46518

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: 1-20
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Groups 1-74 drawn to SEQ ID NOS. 11-58, 60-64, 66, and 68-87, respectively, of claim 3,

This international searching authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2, and 13.3) for the reasons indicated below:

According to the guidelines in Section (f)(i)(a) of Annex B of the PCT Administrative Instructions, the special technical feature as defined by PCT Rule 13.2 shall be considered to be met when all the alternatives of a Markush-group are of similar nature. For chemical alternatives, such as the claimed sequences, the Markush group shall be regarded as being of similar nature when

(A) all alternatives have a common property or activity and

(B)(1) a common structure is present, i.e., a significant structure is shared by all of the alternatives or

(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to an art recognized class of compounds in the art to which the invention pertains.

The instant sequences are considered to be each separate inventions for the following reasons:

The sequences do not meet the criteria of (A), common property or activity. The sequences each behave in a different way in the context of the claimed invention, as evidenced by the differing levels of inhibition of each oligonucleotide listed in table 1. Each member of the class cannot be substituted, one for the other, with the expectation that the same intended result would be achieved. Further, the sequences do not meet the criteria of (B)(1), as they do not share, one with another, a common core structure.

Accordingly, unity of invention between the antisense sequences is lacking and each sequence claimed is considered to constitute a special technical feature. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.